IN THE CLAIMS

Please cancel claim 2 and replace claims 1, 3-19, 22, and 24-26 with the following amended claims. A marked-up version of the amendment, indicating changes in the claims, is attached hereto as Appendix A.

1. (Twice Amended) A polyamide molecule that specifically binds to base pairs in the minor groove of a DNA molecule, said polyamide molecule comprising:

one or more amino acids comprising a moiety selected from the group consisting of N-methylpyrrole, 3-hydroxy-N-methylpyrrole, and N-methylimidazole, wherein one or more of said amino acid(s) are not α-amino acids; and

a positive patch consisting of a rigid group adjacent to a positively charged group, said rigid group comprising a first and a second amino acid; said first amino acid being selected from the group consisting of arginine, proline, lysine, and hydroxyproline; and said second amino acid being selected from the group consisting of proline, glycine, serine, threonine, leucine, isoleucine, valine, alanine, and hydroxyproline.

3. (Amended) The polyamide of claim 2 wherein said first amino acid is arginine and said second amino acid is proline.

4. (Amended) The polyamide of claim 1 wherein the positively charged group comprises a synthetic or naturally occurring amino acid having a net positive charge.

5. (Amended) The polyamide of claim 1 wherein said positively charged group is selected from the group consisting of a primary amino group, secondary amino group, tertiary amino group, quartenary amino group, guanidinium group, and an amidinium group.

6. (Twice amended) The polyamide of claim 1 wherein said positively charged group is selected from the group consisting of arginine, lysine, and histidine.

7. (Amended) The polyamide of claim 1 wherein said positively charged group is arginine.

8. (Amended) The polyamide of claim 1 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

9. (Amended) The polyamide of claim 1 wherein the polyamide has three or four carboxyamide binding pairs.

10. (Amended) The polyamide of claim 1 wherein the polyamide comprises an (R)-2,4-diaminobutyric acid hairpin turn that facilitates specific binding to base pairs in the minor groove of a DNA molecule.

11. (Amended) The polyamide of claim 10 wherein the R-2-amino group is derivatized to form an acid amide.

12. (Twice Amended) The polyamide of claim 1 having the formula:

$$X_1X_2X_3\gamma X_4X_5X_6A$$

wherein γ is $-NH-CH_2-CH_2-CH_2-CONH-$ hairpin linkage derived from γ-aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

X_1/X_6, X_2/X_5, and X_3/X_4 represent three carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of 3-hydroxy-N-methylpyrrole/N-methylpyrrole (Hp/Py), N-methylpyrrole/3-hydroxy-N-methylpyrrole (Py/Hp), N-methylpyrrole/N-methylimidazole (Py/Im), N-methylimidazole/N-methylimidazole (Im/Py), and N-methylpyrrole/N-methylpyrrole (Py/Py) to correspond to the DNA base pair in the minor groove to be bound; and

A represents said positive patch consisting of a rigid group adjacent to a positively charged group.

13. (Amended) The polyamide of claim 12 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

14. (Twice amended) The polyamide of claim 1 having the formula:

$$X_1X_2X_3X_4\gamma X_5X_6X_7X_8A$$

wherein γ is –NH-CH_2-CH_2-CH_2-CONH- hairpin linkage derived from γ-aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

X_1/X_8, X_2/X_7, X_3/X_6, and X_4/X_5 represent four carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of Hp/Py, Py/Hp, Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound; and

A represents said positive patch consisting of a rigid group adjacent to a positively charged group.

15. (Amended) The A polyamide of claim 14 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

16. (Twice amended) The polyamide of claim 1 having the formula:

$$X_1X_2X_3X_4X_5\gamma X_6X_7X_8X_9X_{10}A$$

wherein γ is –NH-CH_2-CH_2-CH_2-CONH- hairpin linkage derived from γ-aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

X_1/X_{10}, X_2/X_9, X_3/X_8, X_4/X_7, and X_5/X_6 represent five carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of Hp/Py, Py/Hp, Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound; and

A represents said positive patch consisting of a rigid group adjacent to a positively charged group.

17. (Amended) The polyamide of claim 16 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

18. (Twice amended) The polyamide of claim 1 having the formula:

$$X_1X_2X_3X_4X_5X_6\gamma X_7X_8X_9X_{10}X_{11}X_{12}A$$

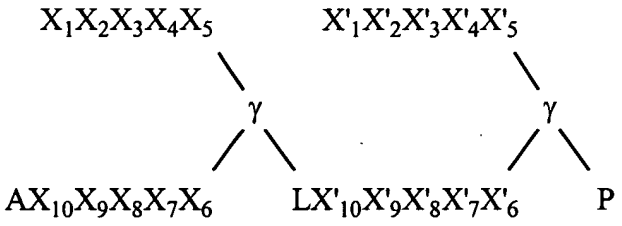
wherein γ is –NH-CH_2-CH_2-CH_2-CONH- hairpin linkage derived from γ-aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

X_1/X_{12}, X_2/X_{11}, X_3/X_{10}, X_4/X_9, X_5/X_8, and X_6/X_7 represent six carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of Hp/Py, Py/Hp, Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound; and

A represents said positive patch consisting of a rigid group adjacent to a positively charged group.

19. (Amended) The polyamide of claim 18 wherein the positive patch comprises the amino acid sequence Arg-Pro-Arg.

22. (Twice Amended) A tandem-linked polyamide having the formula:



wherein γ is - NH-CH_2-CH_2-CH_2-CONH- hairpin linkage derived from γ-aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

X_1/X_{10}, X_2/X_9, X_3/X_8, X_4/X_7, X_5/X_6, X'_1/X'_{10}, X'_2/X'_9, X'_3/X'_8, X'_4/X'_7, and X'_5/X'_6 represent carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of H_p/P_y, P_y/H_p, P_y/I_m, I_m/P_y, and P_y/P_y to correspond to the DNA base pair in the minor groove to be bound;

L represents an amino acid linking group selected from the group consisting of β-alanine and 5-aminovaleric acid (δ);

P represents a polyamide selected from the group consisting of $X_1X_2X_3\gamma X_4X_5X_6$, $X_1X_2X_3X_4\gamma X_5X_6X_7X_8$, $X_1X_2X_3X_4X_5\gamma X_6X_7X_8X_9X_{10}$, and $X_1X_2X_3X_4X_5X_6\gamma X_7X_8X_9X_{10}X_{11}X_{12}$, where X_1-X_{12} are independently selected from the group consisting of β-alanine, pyrrole, hydroxypyrrole and imidazole; and

A represents a positive patch consisting of a rigid group adjacent to a positively charged group.

24. (Amended) The polyamide of claim 1 selected the group consisting of:

ImPyPyPy-γ-PyPyPyPy-β-RPR;

ImImPyPy-γ-ImPyPyPy-β-RPR;

ImPyPyPy-γ-PyPyPyPy-β-RPRRR;

ImImPyPy-γ-ImPyPyPy-β-RPRRR;

ImPyPyPy-γ-PyPyPyPy-β-R;

ImPyPyPy-γ-PyPyPyPy-β-RP;

ImPyPyPy-γ-PyPyPyPy-β-RGR;

ImPyPyPy-γ-PyPyPyPy-β-R^{D}PR;

ImPyPyPy-γ-PyPyPyPy-β-APR;

ImPyPyPy-γ-PyPyPyPy-β-KPR;

ImPyPyPy-γ-PyPyPyPy-β-RPK;

ImPyPyPy-γ-PyPyPyPy-β-C7-RPR; and

the pharmaceutically acceptable salts thereof.

25. (Amended) A method of inhibiting gene expression comprising contacting a regulatory sequence of a gene with the polyamide of claim 1.

26. (Amended) A method of inhibiting gene expression comprising contacting a DNA molecule with the polyamide of claim 1 whereby the DNA molecule is conformationally constrained.